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John W. Boslego

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From 1979 to August 1987, there have been 178 cases of meningococcal disease in Iquique, Chile, a city of about 140000. The attack rate for the last 5 years has been in excess of 20/100000 per year, more than 20 times greater than for the country overall. The mortality rate was 6%. The disease occurred in patients with ages from 4 months to 60 years, but 89% of cases were in patients < 21 years. The largest number of cases were in the age group 5-9 years (n=54, but the highest incidence occurred in children less than 1 year of age (72.8/100000 per year). The male/female ratio was 1.2. Cases occurred all year round with little seasonal variation. Of the 178 cases, 173 were biologically confirmed. Serogroup analysis of strains from 135 patients revealed A=1, B=124, C=10. Forty-four group B strains from 1985-7 were serotyped: 15:P1.3=36, 15:NT=4, 4:P1.3=2, NT:NT=2. Ten of 11 of the outbreak strains tested were sulfadiazine-resistant. This the first recognized outbreak caused by a Gp B:15 strain in South America. It shares many of the characteristics of outbreaks caused by closely related strains in Europe, such as a predilection for older children and adolescents, sulfadiazine-resistance, and
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Serotype-specific outbreak of group B meningococcal disease in Iquique, Chile

C. CRUZ[1], G. PAVEZ[1], E. AGUILAR[1], L. GRAWE[1], J. CAM[1], F. MENDEZ[1], J. GARCIA[2], S. RUIZ[2], P. VICENT[3], I. CANEPA[3], M. MARTINEZ[1], J. BOSLEGO[4], W. ZOLLINGER[4], J. ARTHUR[4] AND D. CAUGANT[5].

[1] *Iquique Health Service, Iquique, Chile*
[2] *Institute of Public Health, Santiago, Chile*
[3] *Ministry of Health, Santiago, Chile*
[4] *Department of Bacterial Diseases, Walter Reed Army Institute of Research, Washington, DC*
[5] *National Institute of Public Health, Oslo, Norway*

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SUMMARY

From 1979 to August 1987, there have been 178 cases of meningococcal disease in Iquique, Chile, a city of about 140000. The attack rate for the last 5 years has been in excess of 20/100000 per year, more than 20 times greater than for the country overall. The mortality rate was 6%. The disease occurred in patients with ages from 4 months to 60 years, but 89% of cases were in patients < 21 years. The largest number of cases were in the age group 5–9 years ($n = 54$), but the highest incidence occurred in children less than 1 year of age (72·8/100000 per year). The male/female ratio was 1·2. Cases occurred all year round with little seasonal variation. Of the 178 cases, 173 were biologically confirmed. Serogroup analysis of strains from 135 patients revealed A = 1, B = 124, C = 10. Forty-four group B strains from 1985–7 were serotyped: 15:P1.3 = 36, 15:NT = 4, 4:P1.3 = 2, NT:NT = 2. Ten of 11 of the outbreak strains tested were sulfadiazine-resistant. This is the first recognized outbreak caused by a Gp B:15 strain in South America. It shares many of the characteristics of outbreaks caused by closely related strains in Europe, such as a predilection for older children and adolescents, sulfadiazine-resistance, and sustained high attack rates. The Iquique strain (B:15:P1.3) belongs to the same genetic clone (ET-5 complex) as the Norway (B:15:P1.16) and the Cuban (B:4:P1.15) strains.

INTRODUCTION

Outbreaks of meningococcal disease have periodically occurred in Chile. The most recent were in 1941–2 and in 1978–9. Between outbreaks, the background incidence of meningococcal disease has remained at 0·3–0·6 cases/100000

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Correspondence and reprint requests should be addressed to John W. Boslego, M.D. US Army Component, AFRIMS, APO San Francisco, CA 96346-5000.

inhabitants per year, similar to that in the USA, England and Wales, and the Netherlands (1·2, 0·9, and 1·5 respectively) [1, 2]. In 1978, outbreaks occurred in Santiago and cities in the south of the country [3]. Serogroup A predominated in the south with an incidence reaching a peak of 21·7 cases/100000 per year; initially serogroup C predominated in Santiago, but over a short period the apparent disease rate rose 2- to 3-fold, serogroup A replaced serogroup C, and the case-fatality rate increased to 35%. Anticipating that a large outbreak, as was being experienced in Brazil and Argentina, might occur, a massive bivalent (A/C) meningococcal vaccination campaign was conducted. Thereafter, meningococcal disease incidence reverted to new background levels (0·8–1·1 cases/100000 per year). At that time, a national surveillance programme and reference laboratory were established at the Institute of Public Health in Santiago to monitor meningococcal disease activity in Chile.

Meningococcal disease in Iquique, an isolated coastal city of about 140000 inhabitants in the north of the country, remained at the national background level until the end of 1982, when serogroup B appeared (six cases in November-December) [4]. Iquique, nestled on a volcanic outcropping between the Pacific Ocean and the desert coastal mountain range of northern Chile at 20 °S latitude, enjoys a moderate maritime climate with zero rainfall. The city is urban (92%) with a population that remains geographically stable. With the appearance of serogroup B, meningococcal disease incidence jumped to over 20 cases per 100000 inhabitants per year and continues at that rate to the present. This report is a description of meningococcal disease in Iquique from 1979 through August 1987.

METHODS

Case definitions

A bacteriologically-proven case was defined as a patient with clinical illness consistent with meningococcal disease from whom *Neisseria meningitidis* was isolated from blood and/or spinal fluid, or Gram-negative diplococci were seen on Gram stain of the spinal fluid. A clinically suspicious case was defined as a patient admitted to the hospital with a clinical diagnosis of meningococcal disease (fever and haemorrhagic rash with or without meningitis), who was treated with appropriate antibiotics, but from whom no organism was isolated from blood or spinal fluid.

Microbiology

Prior to 1981 *N. meningitidis* isolates were identified by colony morphology and Gram stain in Iquique, without further characterization. Beginning in 1981, isolates were regularly sent to the National Reference Laboratory in Santiago for identification, speciation, grouping and sensitivity testing. At the end of 1985, isolates were sent from the reference laboratory to Walter Reed Army Institute of Research in Washington, DC, where the group, type and subtype were determined by a modified dot-blot procedure using monoclonal antibodies [5, 6]. Initially, most of the isolates from Iquique were not subtypable utilizing the available monoclonal antibodies (subtypes 1, 2, 15, 16). Accordingly, a new monoclonal antibody with specificity for the class 1 protein of the Iquique isolates was

prepared as described previously [6]. This new subtype was found to be distinct from all other subtypes and designated P1.3.

The electrophoretic types of 40 meningococcal strains from Chile were analysed using a set of 14 enzymes: malic enzyme, glucose 6-phosphate dehydrogenase, peptidase, isocitrate dehydrogenase, aconitase, NADP-linked glutamate dehydrogenase, NAD-linked glutamate dehydrogenase, alcohol dehydrogenase, fumarase, alkaline phosphatase, indophenol oxidases 1 and 2, adenylate kinase, and an unknown dehydrogenase [7].

Isolates were tested for sulfadiazine sensitivity by a standardized disk method (Difco Laboratories, Detroit, MI). Tests were done in duplicate with known sensitive and resistant strains as controls [8].

Management

All patients in the region suspected of having an infectious or communicable disease were referred for admission to the single regional hospital in Iquique. A high index of suspicion for meningococcal disease in both medical and lay communities led to early recognition and aggressive therapy for suspect cases. A system was established for the immediate telephone notification of clinically suspicious cases to the local health authorities. A home visit was generally made within 24 h of notification for each case. Following collection of epidemiological data, a standard rifampicin chemoprophylaxis regimen was administered to intimate contacts.

RESULTS

Epidemiology

A total of 178 meningococcal disease cases were reported between 1979 and August 1987. One hundred and seventy-three cases were bacteriologically-proven and five cases were clinically suspicious. The outbreak progressed rapidly at the end of 1982 and reached an attack rate of over 20 cases/100000 per year (Fig. 1).

The highest number of cases occurred in the 5–9 years age group (30%), and 79% of cases occurred in children less than 15 years of age. The highest incidence occurred in children less than 1 year (72·8/100000 per year), (Fig. 2). The male:female ratio was 1·2.

Cases totalling 95·5% occurred in the city and 67·3% of cases occurred in the newer, but less affluent, eastern half of the city. Moreover, 33·3% of cases occurred in 4 of the 48 geographic districts of the city, and all 4 had average yearly attack rates of 30–50/100000 per year. Thirteen schools had two or more cases, but the cases within each individual school were separated by more than 6 months in all instances. Two case pairs occurred within families. The secondary cases were in siblings and were separated by 1–6 months. Ten neighbourhoods had two cases each. In two neighbourhoods, the case pairs occurred within 30–40 days of each other. In the remaining eight neighbourhoods, the case pairs were separated by 1–4 years.

Cases occurred throughout the year, but there was a tendency to have more cases in May–July, and November–December, corresponding to the change of season: from fall to winter, and from spring to summer respectively (Fig. 3). However, Iquique has a moderate maritime climate, zero rainfall, and average

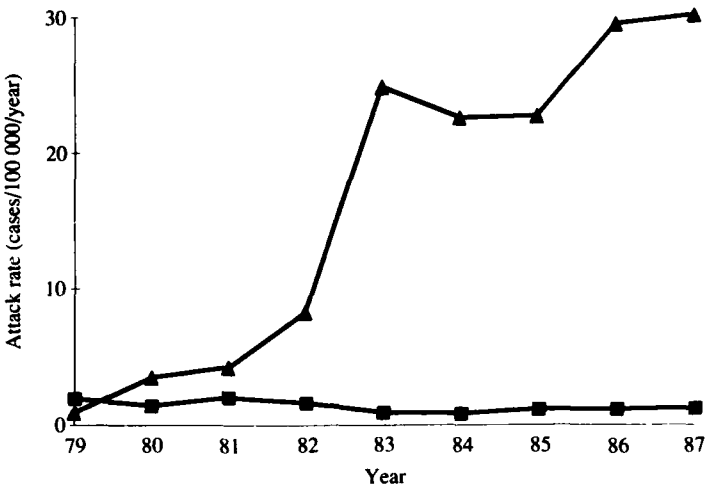

Fig. 1. Meningococcal disease incidence in Iquique (▲), and Chile (■), 1979 through August 1987. Data from Iquique include 178 cases (confirmed or highly suspicious). Attack rates for 1987 are based upon data from January through August, extrapolated to 1 year.

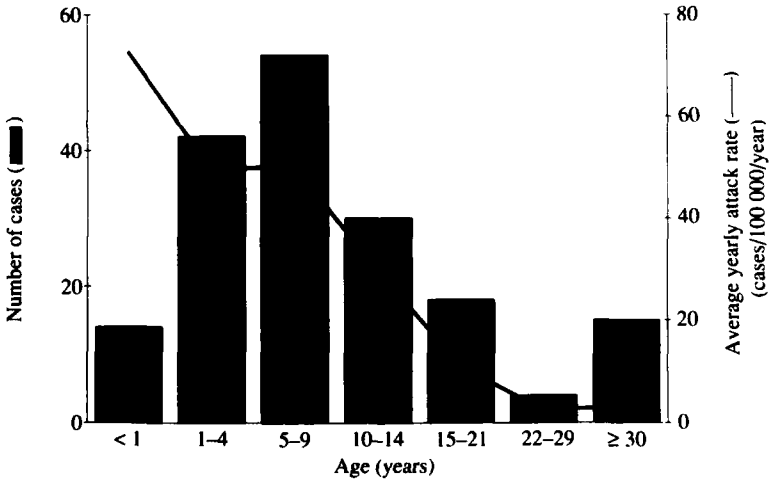

Fig. 2. Age distribution of cases and average yearly age-specific attack rates of meningococcal disease in Iquique, Chile for years 1979 to August 1987. Data include 177 cases (confirmed or highly suspicious). The age of one patient was unknown.

temperatures of 22 °C in summer and 15 °C in winter. The climate is similar all year round.

Clinical features

Of the 178 patients, 174 had sufficient data available to determine a clinical pattern. Fifty-nine had meningitis alone, 98 had meningitis and a haemorrhagic rash, and 17 had meningococcaemia without meningitis (Table 1). There were 10 deaths (5·7% mortality rate) during the study period. Patients with meningococcaemia alone had the worst prognosis (29·4% mortality). Complications in the

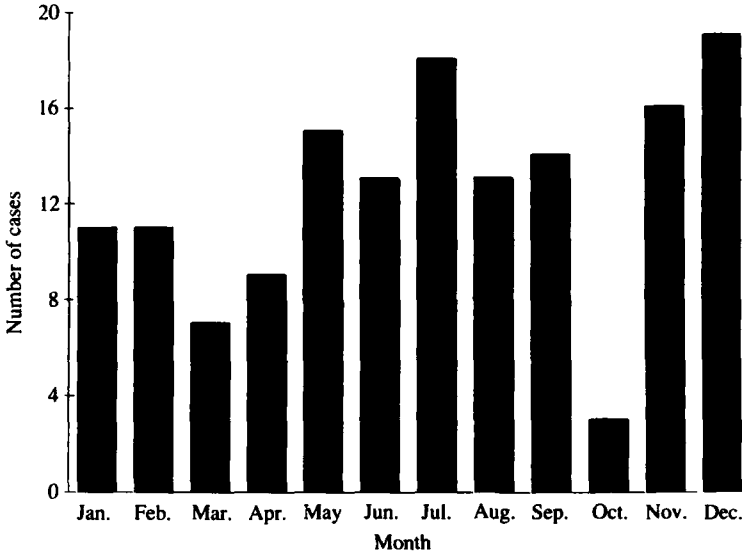

Fig. 3. Monthly distribution of meningococcal disease cases in Iquique, Chile for years 1979–86. Data include 149 cases (confirmed or highly suspicious). Cases occurring in 1987 are not included since the period of analysis ends in August 1987.

Table 1. *Clinical patterns of meningococcal disease in Iquique, Chile**

Clinical pattern	Number	Deaths	Mortality (%)
Meningitis alone, no rash	59	4	6·7
Meningitis and haemorrhagic rash	98	1	1·0
Meningococcaemia without meningitis	17	5	29·4
Total	174	10	5·7

* Data include 174/178 patients with sufficient information to determine clinical pattern.

hospital course were similar to those observed previously [9]. Three patients suffered permanent sequelae of partial or complete deafness.

Microbiology

Neisseria meningitidis was isolated from the blood and/or spinal fluid in 163/178 patients. Ten cases were confirmed solely by the presence of Gram-negative diplococci in the spinal fluid. There was one group A isolate in 1981 and none subsequently; 124 group B, and 10 group C isolates were found throughout the period; and 28 isolates did not survive shipment to the Reference Laboratory (Fig. 4). Thirty-six of 44 (82%) isolates from 1985–7 available for serotyping were B:15:P1.3 (Table 2). Ten of 11 outbreak strains (B:15:P1.3) tested for sulfadiazine sensitivity were found to be sulfadiazine-resistant.

Forty strains were analysed for electrophoretic type by multilocus enzyme electrophoresis in order to relate the Iquique epidemic clone to those strains causing disease in other parts of the world (Table 3). All 23 case strains from Iquique including 3 of a different serotype and 2 that were not subtypeable were

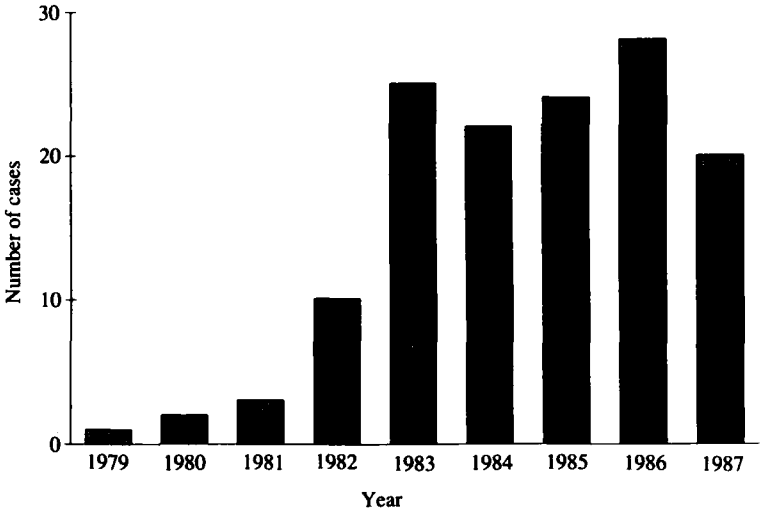

Fig. 4. Meningococcal isolates by serogroup and year in Iquique, Chile. Data are from 163 cases with positive blood or cerebrospinal fluid cultures. Twenty-eight isolates were not subjected to serogrouping. For the 135 isolates that were serogrouped: A = 1 (0·7%); B = 124 (91·9%); C = 10 (7·4%). Data for 1987 include cases from January to August only. Serogroups: A, ▨; B, ■; C, ▩.

Table 2. *Serotypes of group B* Neisseria meningitidis *case isolates, Iquique, Chile, 1985–7 (n = 44)*

Serotype	Number (%)
B:15:P1.3	36 (82)
B:15:NT*	4 (9)
B:4:P1.3	2 (4·5)
B:NT:NT	2 (4·5)

* NT, Non-typable.

of the ET-5 complex. All remaining B:15:P1.3 strains, including 4 throat isolates from Iquique, 5 case isolates from Santiago, and 1 case isolate from Arica, were also of the ET-5 complex.

Outbreak management

In spite of heightened community awareness, early notification, and prompt identification and chemoprophylaxis of intimate contacts of cases, the outbreak continued unabated. Because of the presence of some group C disease, and the availability of an A/C vaccine, a wide scale bivalent (A/C) meningococcal vaccine campaign was carried out in Iquique in 1985.

DISCUSSION

Although serotype-specific group B meningococcal outbreaks have been recognized since the 1960s in North-West Europe, outbreaks of this type in South America are a newly appreciated phenomenon. The Iquique outbreak has been

Table 3. *Serotype, subtype and enzyme type of meningococcal strains from Chile*

City	Source	Strain	Number of strains: Total	ET-5	ET-5 complex*	Other ETs
Iquique	Case	B:15:P1.3	18	16	2	—
		B:15:NT	2	2	—	—
		B:4:P1.3	3	1	2	—
	Throat	B:15:P1.3	4	3	1	—
		B:4:P1.15	1	—	—	1
		29E:4:P1.15	4	—	--	4
Santiago	Case	B:15:P1.3	5	3	2	—
		B:NT:NT	1	—	—	1
		B:2a:P1.15	1	—	—	1
Arica	Case	B:15:P1.3	1	1	—	—
Total			40	26	7	7

* Different from ET-5 at a single enzyme locus.

due to a B:15:P1.3 strain and shares some of the features of the B:15:P1.16 outbreaks reported in North-West Europe: a high attack rate for an extended period (more than 5 years) and the occurrence of disease in older children and young adults. Forty strains from Chile, including 32 isolates from Iquique, were analysed by multilocus enzyme electrophoresis [7, 10]. All case strains from Iquique, as well as B:15:P1.3 case isolates from Santiago and Arica, were found to belong to the ET-5 complex of strains. The Iquique B:15:P1.3 strains, therefore, belong to the same genetic clone as the Norway B:15:P1.16 strains.

Another group B outbreak is also occurring in the Western Hemisphere (Cuba), but the prevalent strain is of a different serotype and subtype (B:4:P1.15) [11]. This strain also belongs to the ET-5 complex [10].

It is possible that the rapid presentation of patients for diagnosis and treatment, and aggressive chemoprophylaxis of contacts has limited spread of disease within the susceptible population, but there has still been no abatement of the outbreak. Interestingly, the strain has also been identified infrequently in other cities in Chile, but so far has failed to cause additional outbreaks.

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